

Poor physical function, pain, and limited exercise: Risk factors for premature mortality in the range of hypertension and smoking, identified on a simple patient self-report questionnaire for usual care

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Figure1_Sokka&Pincus.MDI Figure2_Sokka&Pincus.MDI



Poor physical function, pain, and limited exercise: Risk factors for premature mortality in the range of hypertension and smoking, identified on a simple patient self-report questionnaire for usual care

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ABSTRACT (238 words)

Objective: To analyze poor physical function, pain, limited exercise and smoking, collected on a standard patient self-report questionnaire, to predict 5-year mortality in individuals in a general older population.

Methods: An extended version of a Multidimensional Health Assessment Questionnaire (MDHAQ) was mailed to 2000 subjects in Finland who were randomly identified as a control population for a rheumatoid arthritis cohort. The questionnaire was returned by 1,573 subjects. The questionnaire included scores for baseline physical function, pain, exercise and smoking status, age, and 25 medical conditions, including hypertension. Five-year survival was analyzed according to all baseline variables.

Results: Five-year survival was 94% in all subjects, 98% in subjects with no disease or no acutely life-threatening disease, and 17% in subjects with an acutely life-threatening disease. Hazard ratios in all subjects to die over 5 years were 3.5, 2.2, 5.2 and 4.6 for poor physical function, pain, limited exercise and smoking, respectively, with 5-year survival of 93%, 97%, 93% and 95%, respectively, compared to 91% for hypertension. Each of the four patient history variables predicted mortality at higher levels in individuals who reported <u>no</u> versus an acutely life-threatening condition, in whom the condition dominated prognosis for survival.

Conclusions: Poor physical function, pain, limited exercise, and smoking are potentially modifiable risk factors for premature mortality in the general population, which may be assessed systematically in all individuals in the infrastructure of medical care and health maintenance on a simple standard MDHAQ.

ARTICLE SUMMARY

Article focus:

- To analyze poor physical function, pain, limited exercise and smoking as reversible risk factors to predict 5-year mortality in individuals in a general older population.
- Can the information can be collected as quantitative, standard patient-history scores on a simple, one-page patient self-report questionnaire?
- Are these risk factors are seen in individuals who do not report any potentially acutely life-threatening disease?

Key messages:

- Poor physical function, pain, and limited exercise are potentially modifiable risk factors for premature mortality in the general population.
- These patient history-derived risk factors are in the range of hypertension and smoking as potentially reversible risk factors for mortality.
- Most medical visits do not include any systematic quantitative collection of standard quantitative scores for physical function, pain, exercise status, and even smoking, but these are easily collected on a simple questionnaire.

Strengths and limitations of this study:

Strengths:

- Population-based sample
- Survey returned by 1,573 of 2,000 subjects (79%)
- Questionnaire easily used in any clinical or research setting

Limitations:

- No laboratory tests were available it might be of considerable interest to compare these medical history variables with laboratory tests, such as serum cholesterol, in the prognosis of mortality, and whether a component of the risk may be explained by one or more of the reported medical history variables, or whether the prognosis according to the laboratory test is "explained" by a patient measure.
- All subjects were from Finland, although most data suggest that mortality
 experience in Finland is similar to that found in most Western countries, and
 reports from many countries have indicated that each of these variables is
 prognostic of premature mortality.
- Diagnoses were available only from self-report, which can be inaccurate for certain diagnoses. However, the excess risk according to physical function, pain, and exercise status was greater in subjects who reported no acutely lifethreatening diseases.

INTRODUCTION

Poor physical function,¹⁻⁷ pain,^{3, 8-10} limited exercise,^{11, 12} and smoking^{13, 14} each are significant potentially modifiable risk factors for mortality derived from a medical history. However, these (and other) risk factors for premature mortality derived from a patient history generally are not assessed systematically in most usual medical care and health promotion settings,^{13, 15} unlike blood pressure or serum cholesterol, although they might be associated with similar risks for mortality. This situation may result in part from the absence of a standard simple structured format for recording patient history variables, in contrast to vital signs or laboratory tests.

Medical history information concerning physical function, pain, exercise and smoking status may be collected as standard "scientific" data on a simple self-report questionnaire. A two-page version of a multidimensional health assessment questionnaire (MDHAQ)^{16, 17} (Figure 1) can be completed by patients in 5–10 minutes in any setting, with minimal additional burden on health professionals.¹⁸ Analysis of 5-year survival according to baseline data collected on a questionnaire providing these variables as quantitative scores, as well as review of systems and recent medical history, in a randomly-identified older Finnish population is presented in this report.

METHODS

Subjects

The subjects included 1,523 older individuals in the general population of the Central Finland District. Initially, 2,000 individuals were identified randomly from the Finnish Population Registry as a "control" population for a cohort of 1,500 people with

rheumatoid arthritis who are being monitored for long-term outcomes.¹⁹ The cohort was designed to include 70% females, with mean age of 55 years, but with no selection criteria other than age and sex.

A self-report questionnaire (which included the items in Figure 1, plus additional items designed for further longitudinal research) was mailed to 2,000 randomly-identified older individuals in the general population, and returned by 1,523 (76%). Five years later, in September 2005, the vital status of all subjects was ascertained from the Finnish Population Registry. The study was approved by the Ethics Committees of Jyväskylä Central Hospital and Population Register Centre of Finland.

Self-report questionnaire

A self-report questionnaire mailed to patients included the items on the MDHAQ in Figure 1, and additional queries for a research study. Physical function was queried on a version of the original Health Assessment Questionnaire (HAQ),²⁰ which queries 20 activities of daily living, scored 0–3, with a mean overall physical function score of 0–3; similar results are seen with inclusion of only 10 activities on a MDHAQ.^{16, 17} Pain is assessed on a 10 cm pain visual analog scale (VAS) (0="No pain," 10="Pain as bad as it could be"). The frequency of aerobic exercise is queried with five response options: "≥3 times weekly," "1-2 times weekly," "1-2 times monthly," "no exercise," and "cannot exercise because of health conditions." Smoking status is queried as a response to "Do you smoke cigarettes at this time?" with simple "Yes/No" response options. The presence of 25 health conditions (Table 1), which is not included in the MDHAQ for usual clinical care, was queried as "Which of the following conditions have you ever had

at any time?" listing conditions found in Table 1, with "Yes/No" response options. The standard MDHAQ includes date of birth as well as recent medical history, symptom checklist review of systems, and other variables. ^{21, 22}

Statistical analyses

Survival of all subjects over 5 years was computed according to self-report of each individual condition, age, physical function, pain, exercise frequency, and smoking. Analyses of mortality according to continuous variables were computed as median and mean values, and for dichotomous variables as percentages in each category. Statistical significance was analyzed according to a t-test and analysis of covariance for continuous variables and chi-square test for dichotomous variables.

Kaplan-Meier curves and Cox proportional hazard regression models were computed to analyze time-to-death in subjects according to: *a)* physical function scores (range 0–3) of <1 versus ≥1, indicating moderate difficulty to perform activities of daily living; *b)* pain VAS scores (range 0–100) of ≤40 versus >40, indicating moderate pain; *c)* frequency of physical exercise of "1 or more times weekly" versus "less than once weekly"; *d)* current smoking status, analyzed as yes or no. Multivariate models were analyzed for physical function and pain as continuous variables, as well as according to clinical cutpoints that could highlight possible severe problems, such as physical function of ≥1.0 versus <1 on a scale of 0-3, and pain of >40 versus ≤40 on a 0-100 visual analog scale (VAS). Some analyses were stratified according to age, and multivariate computations were adjusted for age, sex, and type of health condition.

Survival was also analyzed for subjects classified into three categories on the basis of results of the survey: no reported health condition; one or more condition(s) but no acutely life-threatening condition; and one or more acutely life-threatening condition(s), as defined by the findings described in Results. Few deaths occurred in those who reported no health condition, and further analyses were performed in two categories: no condition or no acutely life-threatening condition versus one or more acutely life-threatening condition(s).

Role of the funding source

No specific funding source was available for these studies. The authors are solely responsible for the study design; collection, analysis and interpretation of data; writing the report; and a decision to submit the paper for publication.

RESULTS

Overall mortality in the cohort

The mean age of the 1,523 individuals in the study population was 55 years (range 30-91 years), and 72% were females. Among the 1,523 subjects, 92 (6.0%) died over the subsequent 5 years. Eight of 25 health conditions were found associated with 5-year mortality rates of 19% or more, and were classified as "acutely life-threatening diseases," i.e., coronary artery disease, other heart diseases, chronic kidney disease, chronic bronchitis, chronic leg ulcers, diabetes, cancer and stroke. The 17 other conditions with subsequent 5-year mortality rates of 17% or less were classified as "non-acutely life-threatening diseases," i.e., hypertension, peptic ulcer, inflammatory gut

disease, asthma, thyroid disease, Parkinson's disease, epilepsy, other neurologic diseases, chronic back pain, fibromyalgia, psoriasis, psychiatric diseases, alcoholism, osteoarthritis, musculoskeletal trauma, rheumatoid arthritis and ankylosing spondylitis.

The 92 deaths included 8 of 429 (1.9%) who had reported no health condition, 21 of 728 (2.9%) with a non-acutely life-threatening condition, and 63 of 366 (17.2%) with one or more acutely life-threatening conditions (Table 1) (some patients had 2 or 3 such conditions, so total mortality was less than 19%). The 8 subjects with no health condition and 21 with no acutely life-threatening conditions were pooled for further mortality analyses as 29 (2.5%) of 1,157 subjects with no condition or no acutely life-threatening condition who died within 5 years. The mean baseline age of all patients who survived or died over the 5-year period was 54 and 75 years, respectively (p <0.001) (Table 2), including 51 and 69 years in subjects with no conditions or no acutely life-threatening conditions (p <0.001), and 65 and 77 years in subjects with an acutely life-threatening condition (p <0.001).

Survival according to medical history variables

Cumulative survival in the entire population differed according to physical function scores: 98% with scores <1 (on a 0-3 scale) survived versus 93% with scores ≥1 (Figure 2). Survival was 99% in those with pain VAS scores ≤4 versus 97% in those with pain scores >4. Survival was >99% in those who exercised more than once weekly, 97% in those who exercised once weekly, and 93% in those who did not exercise. Survival was 98% in non-smokers versus 95% in smokers (Figure 2). Further analyses of survival according to each of the four variables are presented below.

Physical function scores and mortality risk

Mean physical function scores were 0.27 (on a scale of 0–3) in all subjects, including 0.20 in those who survived and 1.4 in those who died over the 5-year period (p <0.001) (Table 2). In the 1,257 subjects with no conditions or no acutely life-threatening conditions, mean physical function scores were 0.16, including 0.13 for those who survived and 1.1 for those who died (p <0.001) (Table 2). In the 366 subjects with acutely life-threatening conditions, mean physical function scores were 0.63, including 0.45 in those who survived and 1.5 in those who died (p <0.001) (Table 2). The hazard ratio and 95% confidence interval (CI) for mortality over 5 years for physical function scores \geq 1 (on a scale of 0–3), was 3.5 (95% CI: 2.1–5.1) for all subjects, 4.5 (95% CI: 1.6–12.6) for those with non-acutely life-threatening conditions, and 3.1 (95% CI: 1.8–5.5) for those with acutely life-threatening conditions (Table 3).

Pain scores and mortality risk

The mean pain score was 20 (on a scale of 0–100) in all subjects, including a mean level of 19 in those who survived compared to 38 in those who died over the next 5 years (p <0.001) (Table 2). The mean pain score in individuals with no condition or no acutely life-threatening condition was 16, including 16 in those who survived compared to 27 in those who died (p = 0.020) (Table 2). The mean pain score in subjects with an acutely life-threatening condition was 34, including 32 in those who survived compared to 43 in those who died over the next 5 years (p = 0.008). The hazard ratio (with 95% CI) for mortality over 5 years if pain scores were >40 compared to \leq 40 (on a scale of 0–

100) was 2.2 (95% CI: 1.3–3.5) for all subjects (Table 3), 3.1 (95% CI: 1.2–8.3) for those with non-acutely life-threatening conditions, but 1.5 (95% CI: 0.9–2.8) for those with acutely life-threatening conditions, not meeting the p<0.05 criterion (p <0.16).

Exercise frequency and mortality risk

Among all individuals, 28% exercised less than once per week, including 26% of those who survived and 76% of those who died over the 5 years (Table 2). Among subjects with no conditions or no acutely life-threatening conditions, 25% exercised less than once per week, including 24% who survived versus 63% who died (Table 2). Among subjects who had an acutely life-threatening condition, 40% exercised less than once per week, including 33% who survived and 82% who died. The hazard ratio (with 95% CI) for death over 5 years among subjects who exercised less than once per week compared to those who did exercise at least once per week was 5.2 (95% CI: 3.1–8.9) for all subjects, 4.9 (95% CI: 1.8–13) for those with non-acutely life-threatening conditions, and 4.7 (95% CI: 2.3–9.6) for those who had an acutely life-threatening condition (p <0.001 for all comparisons) (Table 3).

Smoking and mortality risk

Current smoking was reported by 17% of subjects, including 17% who survived versus 19% who died over the 5-year period (p=0.61) (Table 2). Among those with no condition or no acutely life-threatening condition, 19% were smokers, including 18% who survived versus 28% who died (p=0.27). Among those who had acutely life-threatening conditions, 13% were smokers, including 12% who survived versus 15%

who died (p = 0.59). Among all subjects, people who smoked at baseline had a 4.6-fold higher hazard ratio (95% CI: 2.5–8.6) to die within 5 years compared to nonsmokers (p <0.001), including a hazard ratio of 7.4 (95% CI: 2.1–25) among people with a condition that was not acutely life-threatening, and 3.3 (95% CI: 1.5–7.3) among those who had an acutely life-threatening condition (Table 3).

Multivariate Cox regression analyses

The four variables studied are not independent, and multivariate regression analyses were performed (Table 4). In the entire cohort, physical function, exercise and current smoking were each significant independent predictors of 5-year mortality, while pain was not significant, i.e., explained by the other variables (Table 4). In individuals younger than age 55 who had no acutely life-threatening condition, pain and smoking were significant independent predictors of mortality, and physical function and exercise were not significant; no medical history variable was significant in multivariate analyses. In individuals 55 years old and older who had no acutely life-threatening condition, functional status was the only significant predictor of mortality, whereas both functional status and lack of exercise (but not pain or smoking) were independent statistically significant predictors in individuals over age 55 who had an acutely life-threatening condition (Table 4).

DISCUSSION

The data presented in this report confirm and extend a large number of reports, (only a few of which are cited here) that poor physical function, ¹⁻⁷ pain, ^{3, 8-10} limited

exercise,^{11, 12} and smoking¹⁴ predict premature mortality. Smoking¹⁴ and limited exercise^{11, 12, 23} are more widely recognized as predictors of premature death than poor physical function^{2, 7} and pain.^{3, 9, 10} Nonetheless, these four medical history variables are usually not collected in everyday medical care – even smoking status often remains unknown,²⁴ although some evidence of improvement has been reported.²⁵

The new information here is that these medical history data can be collected easily in a 1-page (2-sided) MDHAQ-type self-report format (Figure 1), which is easily completed by patients while waiting to see a health professional.¹⁷ A version of this questionnaire has been incorporated into the infrastructure of the authors' usual clinical care²⁶ and many other settings. Collection of these data involves no additional effort on the part of a physician or an assistant, and can be adapted to any clinical, health maintenance or research setting.

In the reported cohort of 1,523 older people from the general Finnish population, survival was 93% in subjects who reported poor physical function and limited exercise, compared to 95% in smokers, 97% in those who reported pain, and 91% in those who reported hypertension, versus 98-99% in other subjects. It could be suggested that one or more of the four patient history variables, which are correlated with one another, might not be necessary in clinical care. However, clinical care of individual patients necessarily addresses multiple variables that might be correlated significantly – e.g., blood pressure, cholesterol, glucose – with evidence that each may contribute to a poor outcome. The data establish that each of these variables identifies a potentially modifiable important indicator of higher mortality risk in affected subjects.

The four medical history risk factors for mortality – poor physical function, pain, limited exercise and smoking – may be regarded as "vital signs" in care of chronic diseases and health maintenance. These "vital signs" are analogous to traditional vital signs in acute care, such as pulse and temperature. Pain^{27, 28} and smoking status¹⁴ have been advocated as "vital signs," introducing a concept that a vital sign may be derived from a medical history, rather than from physical examination. Vital signs often confirm impressions of the clinician, but provide standard quantitative data which may be monitored from one encounter to another more accurately than through narrative descriptions.

Vital signs that identify risk of premature mortality may provide data to analyze whether interventions to improve values of variables such as physical function or pain will improve survival, as seen for exercise, smoking, blood pressure, and cholesterol. It may also be desirable to include these medical history variables in research and clinical analyses of any risk factor for long-term mortality, to ascertain the extent to which they may modify biomedical, genetic and physiologic risk factors in prediction of long-term mortality.

Poor physical function has been characterized extensively as a predictor of long-term mortality.^{2, 7} In patients with rheumatoid arthritis, physical function in the format of the questionnaire in this study is as significant as or more significant than radiographic scores or laboratory tests to predict mortality over 5-15 years.^{1, 3, 7} Poor functional status also has been reported to predict mortality in patients with congestive heart failure as strongly as ejection fraction,⁴ in patients with AIDS as strongly as T4/T8 lymphocyte ratios,⁵ in elderly patients,⁶ and in the general population over 2 years.⁷

Pain is one of the primary reasons people seek medical care,²⁹ and is regarded as a marker for conditions that predispose to mortality, including cardiovascular disease and cancer.¹⁰ In this study, the relative risk of death according to pain (as well as the other three patient self-report measures) was explained only in small part by the presence of acutely life-threatening diseases, and was considerably higher in individuals who reported <u>no</u> acutely life-threatening disease. Previous reports also have indicated that high levels of pain predict premature mortality independent of disease,^{3,9,10} as was found in the present study. Furthermore, quantitation of pain on a simple visual analog scale (VAS) can improve accuracy of assessment and monitoring of pain in any condition.

Physical exercise in prevention of long-term mortality has been characterized extensively in the literature. Physiologic measures may provide more accurate prediction of mortality than self-report, but the expense of collecting self-report data is considerably lower than a physiologic measure. Exercise appears salutary for all human beings, but patient exercise frequency is not obtained regularly at most physician encounters.

As noted, smoking is widely recognized as a predictor of premature mortality, ¹⁴ yet physicians often do not include a query about smoking. ²⁴ Smoking cessation appears more a result of extensive public-health efforts than attributable to medical care, though physicians' reminders have been moderately successful. ¹⁵ Physician and public health interventions regarding physical function, pain and exercise, to a similar extent as smoking cessation efforts, could be as effective in promoting health as pharmacologic interventions for recognized risk factors such as hypertension or hyperlipidemia.

Several limitations are seen to this study. No laboratory tests were available – it might be of considerable interest to compare these medical history variables with laboratory tests, such as serum cholesterol, in the prognosis of mortality, and whether a component of the risk may be explained by one or more of the reported medical history variables. All subjects were from Finland, although most data suggest that mortality experience in Finland is similar to that found in most Western countries, and reports from many countries have indicated that each of these variables is prognostic of premature mortality. Diagnoses were available only from self-report, which can be inaccurate for certain diagnoses.³⁰ Nonetheless, most of the excess risk according to these medical history variables was not seen in patients with acutely life-threatening diseases, which ironically may be over-reported in many situations.

In conclusion, risk factors for premature mortality from a medical history – including physical dysfunction, pain, limited exercise, and smoking – may be assessed in a standard systematic format on a simple patient self-report questionnaire. This questionnaire can be used at any visit in usual care, health maintenance, and clinical research. More information concerning possible modification of these risk factors through therapeutic intervention could advance the quality of life and longevity in many individuals, and general public health in populations.

Authors' statement of contributions:

Design: Sokka and Pincus

Supervision of Data Collection: Sokka

Analyses: Sokka and Pincus

Preparation of manuscript: Pincus and Sokka

Funding: No specific funding source was available for these studies. The authors are solely responsible for the study design; collection, analysis and interpretation of data; writing the report; and a decision to submit the paper for publication.

Competing interest: Dr. Sokka and Dr. Pincus report no competing interest.

Ethics approval: The study was approved by the Ethics Committees of Jyväskylä Central Hospital and Population Register Centre of Finland.

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Table 1. Prevalence of conditions in older general population. Baseline scores for pain and functional capacity on health assessment questionnaire (HAQ), according to status at 5 years.

Condition	N	%	Mean Age	% who died over 5 years
Reported acutely life-threat	tening co	ndition		
Chronic leg ulcer Stroke Chronic kidney disease Chronic bronchitis Other heart disease Diabetes Cancer Coronary artery disease	3 16 10 17 146 103 74 135	0.2% 1.0% 0.7% 1.1% 9.6% 6.8% 4.9%	78 71 64 71 69 65 67 73	33% 31% 30% 29% 23% 23% 22% 19%
Reported non-acutely life-t	hreatenin	g condition		
Rheumatoid arthritis Other neurologic disease Parkinson's disease Alcoholism Epilepsy Osteoarthritis Peptic ulcer Psychiatric disease Musculoskeletal trauma Thyroid disease Hypertension Chronic back pain Ankylosing spondylitis Psoriasis Asthma Fibromyalgia Inflammatory gut disease	58 31 7 18 10 370 67 61 182 99 454 373 14 26 130 56 19	3.8% 2.0% 0.5% 1.2% 0.7% 24% 4.4% 4.0% 11.9% 6.5% 30% 25% 0.9% 1.7% 8.5% 3.7% 1.2%	68 65 70 52 57 66 62 54 58 64 62 59 59 59 55 59	17% 16% 14% 11% 10% 10% 10% 9.8% 9.3% 9.1% 8.8% 7.2% 7.1% 3.8% 3.1% 1.8% 0
No reported conditions	429	28%	47	1.9%

Table 2. Mean (standard deviation) values for age, physical function and pain, and percentage of patients who exercise rarely or smoke, according to type of condition and vital status 5 years after baseline.

	All subjects	With no acutely life- threatening condition or no condition	With acutely life- threatening condition
Age in years			
Total	55 (15)	52 (13)	67 (14)
Alive	54 (14)	51 (13)	65 (13)
Dead	75 (13)	69 (15)	77 (12)
p value	< 0.001	<0.001	< 0.001
Physical function	າ (0-3)		
Total	0.27 (0.60)	0.16 (0.50)	0.63 (0.86)
Alive	0.20 (0.46)	0.13 (0.35)	0.45 (0.68)
Dead	1.4 (1.1)	1.1 (1.2)	1.5 (1.1)
p value	< 0.001	<0.001	< 0.001
Pain (0-100)			
Total	20 (24)	16 (21)	34 (29)
Alive	19 (24)	16 (21)	32 (28)
Dead	38 (30)	27 (27)	43 (29)
p value	< 0.001	0.015	< 0.008
Exercise <once p<="" td=""><td>oer week</td><td></td><td></td></once>	oer week		
Total	28.4%	24.8%	40.3%
Alive	25.8%	24.0%	32.5%
Dead	75.9%	62.5%	81.8%
p value	< 0.001	<0.001	<0.001
Current smoker a	at baseline		
Total	17.1%	18.5%	12.8%
Alive	17.0%	18.3%	12.4%
Dead	19.2%	28.0%	15.1%
p value	0.61	0.21	0.59

< 0.001

Table 3. Hazard ratios (95% CI) for 5-year mortality in older general population – analyses adjusted for age and sex.

All subjects			
	% of subjects with poor status	<u>HR (95% CI)</u>	p value*
Physical function ≥1.0 (vs <1.0)	10%	3.5 (2.1 to 5.7)	<0.001
D: 40 / 40)	000/	0.0 (4.0 +- 0.5)	0.000

Pain >40 (vs ≤40) 20% 2.2 (1.3 to 3.5) 0.002 Exercise <1 time/week (vs ≥1 time/week) 28% 5.2 (3.1 to 8.9) <0.001

17%

4.6 (2.5 to 8.6)

Subjects with no acutely life-threatening conditions

Current smoking (vs not smoking)

	% of subjects with poor status	HR (95% CI)	p value*
Physical function ≥1.0 (vs <1.0)	5%	4.5 (1.6 to 13)	0.004
Pain >40 (vs ≤40)	14%	3.1 (1.2 to 8.3)	0.024
Exercise <1 time/week (vs ≥1 time/week)	25%	4.9 (1.8 to 13)	0.001
Current smoking (vs not smoking)	18%	7.4 (2.1 to 25)	0.002

Subjects with acutely life-threatening condition

	% of subjects with poor status	HR (95% CI)	p value*
Physical function ≥1.0 (vs <1.0)	25%	3.1 (1.8 to 5.5)	<0.001
Pain >40 (vs ≤40)	40%	1.5 (0.9 to 2.8)	0.16
Exercise <1 time/week (vs ≥1 time/week)	40%	4.7 (2.3 to 9.6)	<0.001
Current smoking (vs not smoking)	13%	3.3 (1.5 to 7.3)	0.003

^{*} adjusted for age and sex

Table 4. Multivariate model: Hazard ratios (95% CI) for 5-year mortality

FIGURE LEGENDS

Figure 1. Multidimensional health assessment questionnaire (MDHAQ). The front page **(A)** includes 10 activities for function, two visual analog scales (VAS) for pain and patient global estimate of status, and a self-report joint count from a rheumatoid arthritis disease activity index (RADAI). Scoring templates for these measures are available on the right-hand side of the page. An index of the three patient-reported measures, routine assessment of patient index data (RAPID3), can be calculated from an MDHAQ in fewer than 10 seconds. The reverse side **(B)** includes a review of systems, fatigue visual analog scale (VAS), recent medical history, queries about change in global status and frequency of exercise, and demographic data (not included in scoring, but providing useful data in clinical care).

Figure 2. Kaplan Meier survival for mortality according to **A)** functional capacity (HAQ ≥1 vs. <1), **B)** pain (>4.0 vs. ≤4.0), **C)** frequency of physical exercise and **D)** smoking status, over 5 years.

Multi-Dimensional Health Assessment Questionnaire (R808-NP2)

This questionnaire includes information not available from blood tests, X-rays, or any source other than you. Please try to answer each question, even if you do not think it is related to you at this time. Try to complete as much as you can yourself, but if you need help, please ask. There are no right or wrong answers.

Please answer exactly as you think or feel. Thank you.

Without With With UNABLE To Do	1. Please check $()$ the ONE best answer for y	our abilities	at this	time:				FOR OFFICE USE ONLY
a. Dress yourself, including tying shoelaces and doing buttons? b. Get in and out of bed? c. Lift a full cup or glass to your mouth? d. Walk outdoors on flat ground? d. Walk outdoors on flat ground? d. Walk outdoors on flat ground? e. Wash and dry your entire body? e. Wash and dry your entire body? f. Bend down to pick up clothing from the floor? g. Turn regular faucets on and off? f. Bend down to pick up clothing from the floor? g. Turn regular faucets on and off? f. Get in and out of a car, bus, train, or airplane? i. Walk two miles or three kilometers, if you wish? i. Walk two miles or three kilometers, if you wish? i. Walk two miles or three kilometers, if you wish? j. Participate in recreational activities and sports as you would like, if you wish? k. Get a good night's sleep? i. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? o 1.1 2.2 3.3 m. Deal with feelings of depression or feeling blue? None Mild Moderate Severe None Mild Moderate Se	OVER THE LAST WEEK		The second second		The Assessment of the State of		1881000000	The second second second second
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Figure 1A

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The state of the s	ompared to ONE WEEK AGO? Ple (2), the Same \Box (3), Worse \Box (4)	Giana and the control of the control	T 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	o
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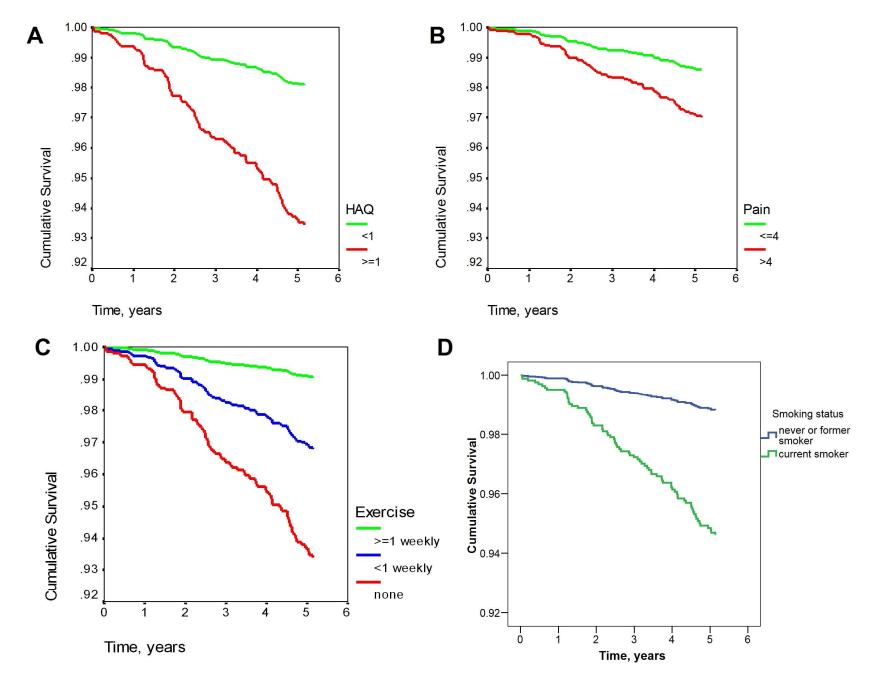


Figure 2. Kaplan Meier survival for mortality according to **A)** functional capacity (HAQ ≥1 vs. <1), **B)** pain (>4.0 vs. ≤4.0), **C)** frequency of physical exercise and **D)** smoking status, over 5 years.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6
		(b) For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	6
measurement		comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7-8
		(b) Describe any methods used to examine subgroups and interactions	7-8
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	7
		(e) Describe any sensitivity analyses	NA
Results	•		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed	5

	1		
		eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	8
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	8
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	3, 12-13
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	4, 12-13
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	17
		which the present article is based	

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.



Poor physical function, pain, and limited exercise: Risk factors for premature mortality in the range of smoking or hypertension, identified on a simple patient self-report questionnaire for usual care

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Poor physical function, pain, and limited exercise: Risk factors for premature mortality in the range of smoking or hypertension, identified on a simple patient self-report questionnaire for usual care

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Word Count: 3,254

Running title: Function, pain, exercise and smoking predict mortality

Key words: pain, functional disability, self-report, population

ABSTRACT (250 words)

Objective: To analyze poor physical function, pain, limited exercise and smoking, assessed in a patient-friendly self-report questionnaire format that has been completed by every patient at every visit over 20-30 years in the authors' and other usual care settings, to predict 5-year mortality in a general older population.

Methods: An extended version of a Multidimensional Health Assessment Questionnaire (MDHAQ) was mailed to 2000 subjects in Finland, identified as a randomly-selected control cohort for a rheumatoid arthritis cohort. The questionnaire included queries concerning baseline physical function, pain, exercise and smoking status, identical to the clinic version, as well as age and 25 medical conditions. Five-year survival was analyzed according to descriptive statistics, Kaplan-Meier curves and Cox regressions.

Results: The questionnaire was returned by 1,523 subjects (76%). Five-year survival was 94% in all subjects, 98% in subjects with no disease or no acutely life-threatening disease, and 17% in subjects with an acutely life-threatening disease. Hazard ratios for 5-year mortality were 3.5 for poor physical function, 2.2 for pain, 5.2 for limited exercise, and 4.6 for smoking (p<0.01); 5-year survivals were 93%, 97%, 93% and 95%, respectively, compared to 91% for hypertension. Each of the four patient history variables predicted mortality at higher levels in subjects who reported <u>no</u> versus one or more acutely life-threatening conditions.

Conclusions: Poor physical function, pain, limited exercise, and smoking can be assessed systematically on a simple standard MDHAQ, to identify potentially modifiable risk factors for premature mortality in the infrastructure of usual medical care and health maintenance.

ARTICLE SUMMARY

Article focus:

- A simple, one-page patient self-report questionnaire to assess systematically
 physical function, pain, and limited exercise, and smoking has been completed
 by all patients at all visits in 5-10 minutes in routine care in several rheumatology
 clinical settings for 20-30 years, including those of the authors,.
- Responses on this questionnaire indicating poor physical function, pain, and limited exercise have been documented as significant prognostic markers for premature mortality in patients with rheumatoid arthritis (RA), with greater significance than radiographs or laboratory tests.
- Questionnaire responses in an older cohort from the general population,
 identified from a population register as a control cohort for a rheumatoid arthritis
 cohort, indicated that poor physical function, pain, and limited exercise also
 predicted 5-year mortality significantly, in the range of smoking and hypertension.

Key messages:

- Poor physical function, pain, and limited exercise are potentially modifiable risk factors for premature mortality in the general population, in a similar range as smoking and hypertension.
- A systematic assessment of these patient history variables is not included at
 most medical visits, in contrast to blood pressure or serum cholesterol, in part as
 most available questionnaire formats appear to add to the burden of care for
 patients and doctors.

- Scores in a simple format on a questionnaire which is completed by patient self-report in 5-10 minutes provide quantitative data concerning physical function, pain, exercise status, and smoking as significant risk factors for mortality, with virtually no additional work on the part of a health professional, to ensure that data are available for clinical review.
- Poor physical function, pain, and limited exercise are more significant in prognosis of death over 5 years in individuals who do <u>not</u> versus do report one or more potentially acutely life-threatening diseases.

Strengths and limitations of this study:

Strengths:

- Population-based subjects
- Survey returned by 1,523 of 2,000 subjects (76%)
- Questionnaire easily completed by patient self-report in 5-10 minutes in any clinical or research setting, or even at home

Limitations:

- No laboratory tests were available it would be of interest to compare medical
 history variables with laboratory tests, such as serum cholesterol, in the
 prognosis of mortality, and whether a component of the risk according to the
 laboratory test may be "explained" in part by a patient history measure.
- All subjects were from Finland, although most data suggest that mortality
 experience in Finland is similar to that found in most Western countries, and
 reports from other countries have indicated that poor physical function, pain and
 limited exercise are prognostic of premature mortality. Furthermore, a response

- rate of >75% from the general population might be unlikely in most countries, and may be unique to Finland.
- Diagnoses were available only from self-report, which can be inaccurate for certain diagnoses. However, the excess risk according to poor physical function, pain, and limited exercise was greater in subjects who reported no versus any acutely life-threatening diseases.
- Actual survey includes more queries, and is not identical to that used in clinical settings, although actual queries about 4 risk factors are identical in clinical and study format.

INTRODUCTION

Poor physical function¹⁻⁷, pain ^{3, 8-10}, limited exercise ^{11, 12}, and smoking ^{13, 14} each are potentially-modifiable significant risk factors for mortality derived from a medical history. However, these risk factors generally are not assessed systematically or even available at most patient visits in usual medical care and health promotion settings ^{13, 15}. By contrast, blood pressure and serum cholesterol are recorded carefully at most visits in contemporary routine care settings and health maintenance, although the patient-history-derived variables may be in a similar range as risk factors for mortality.

One reason that patient history variables are not available in most care settings may be that reported data generally have been collected in complex, non-standard formats, which add to the burden of usual care. Therefore, a simple format for systematic collection of data concerning physical function, pain, exercise status, and smoking in the infrastructure of usual care, with minimal additional effort on the parts of patients and health professionals, could provide a useful advance.

A simple, two-sided/one-page multidimensional health assessment questionnaire (MDHAQ) ^{16, 17} (Figure 1) has been completed at every visit of every patient for 20-30 years in clinical settings of the authors, as well as other rheumatology clinical settings over many years ¹⁸⁻²¹. This questionnaire is readily accepted by patients, and completed in 5–10 minutes while waiting to see the doctor ²¹. Responses to MDHAQ queries concerning physical function, pain, exercise status, and smoking are prognostic of premature mortality in patients with rheumatoid arthritis (RA) ²². Since the MDHAQ format could facilitate availability of the information to any health professional caring for any individual patient, it appeared of interest to analyze whether responses concerning

these variables on this simple questionnaire (in contrast to lengthy questionnaires used in research studies) would be prognostic of 5-year mortality in the general population.

A cohort of 1,523 individuals from a normal older Finnish population had been assembled as a "control group" to be monitored over long periods in comparison with a cohort of RA patients ^{7, 23, 24}. These individuals had completed a questionnaire with MDHAQ queries (used in usual clinical care) for quantitative physical function, pain, exercise frequency and smoking. An earlier report indicated that scores for physical function, but not for pain, were prognostic for mortality 2 years later in this cohort, but the data did not include exercise status and were not adjusted for specific comorbidities, including the presence of acutely life-threatening diseases ⁷. In this report, we present analyses of 5-year survival according to baseline physical function, pain, exercise status, smoking and disease data collected on this questionnaire, in this randomly-identified older Finnish population.

METHODS

Subjects

The subjects were 1,523 older individuals identified in the general population of the Central Finland District. Initially, in the year 2000, the Finnish Population Register Centre identified 2,000 individuals from the general population as a "control" population for a cohort of 1,500 patients with rheumatoid arthritis who are being monitored for long-term outcomes ²³. The cohort was designed to include 70% females, with mean age of 55 years, but otherwise was identified randomly from the general population with no selection criteria other than age and sex.

A self-report questionnaire which included the items in Figure 1 in an identical format, plus additional items designed for further longitudinal research, was mailed to the 2,000 older individuals, identified randomly in the general population from the Finnish Population Register. The questionnaire was returned by 1,523 subjects (76%). Earlier reports two years after baseline indicated that functional status was considerably poorer in age-matched patients with RA than in the general population ²³; that poor physical function not analyzed according to possible diseases, but not pain, was associated with increased mortality rates in both RA patients and the general population⁷; and that significantly higher mortality rates were seen in individuals who did not return the questionnaire ²⁴. Five years after the baseline assessment, in September 2005, the vital status of all subjects was ascertained from the Finnish Population Register. The study was approved by the Ethics Committees of Jyväskylä Central Hospital and Population Register Centre of Finland.

Self-report questionnaire

The self-report questionnaire mailed to subjects in the general population included the items on the MDHAQ in Figure 1, and additional queries concerning diagnoses and demographic data for a research study. Physical function was queried on a version of the original Health Assessment Questionnaire (HAQ) ²⁵, which queries 20 activities of daily living, scored 0–3, with a mean overall physical function score of 0–3; similar results are seen with inclusion of only 10 activities on a MDHAQ ^{16, 17}. Pain was assessed on a 10 cm pain visual analog scale (VAS) (0="No pain," 10="Pain as bad as it could be") derived initially from Huskisson ²⁶. The frequency of aerobic

exercise was queried with five response options: "≥3 times weekly," "1-2 times weekly," "1-2 times monthly," "no exercise," and "cannot exercise because of health conditions." Smoking status was queried as a response to "Do you smoke cigarettes at this time?" with simple "Yes/No" response options. A list of 25 health conditions (Table 1), which is not included in the MDHAQ for usual clinical care, was included on the study questionnaire. Subjects were queried: "Which of the following conditions have you ever had at any time?" with "Yes/No" response options. The standard MDHAQ includes date of birth as well as recent medical history, symptom checklist review of systems, and other variables in a 2-sided, one-page format ^{27, 28}.

Statistical analyses

Data concerning survival of all subjects over 5 years was obtained from the Finnish Population Register Centre in 2005, and was computed according to self-report of each individual condition, age, physical function, pain, exercise frequency, and smoking. Analyses of mortality according to continuous variables were computed as median and mean values, and for dichotomous variables as percentages in each category. Statistical significance was analyzed according to a t-test and analysis of covariance for continuous variables and chi-square test for dichotomous variables.

Survival was analyzed for subjects classified into three categories on the basis of results of the survey: no reported health condition; one or more condition(s) but no acutely life-threatening condition; and one or more acutely life-threatening condition(s), as defined by the findings described in Results. Few deaths occurred in those who reported no health condition, and further analyses were performed in two categories: no

condition or no acutely life-threatening condition versus one or more acutely life-threatening condition(s).

Kaplan-Meier curves and Cox proportional hazard regression models were computed to analyze time-to-death in subjects according to: *a)* physical function scores (range 0–3) of <1 versus ≥1, indicating moderate difficulty to perform activities of daily living; *b)* pain VAS scores (range 0–100) of ≤40 versus >40, indicating moderate pain; *c)* frequency of physical exercise of "1 or more times weekly" versus "less than once weekly"; *d)* current smoking status, analyzed as yes or no. Multivariate models were analyzed for physical function and pain as continuous variables, as well as according to clinical cutpoints that could highlight possible severe status, such as physical function of ≥1.0 versus <1 on a scale of 0-3, and pain of >40 versus ≤40 on a 0-100 visual analog scale (VAS). Certain analyses were stratified according to age, and multivariate computations were adjusted for age, sex, and type of health condition – acutely life-threatening versus non-acutely life-threatening or none.

Role of the funding source

No specific funding source was available for these studies. The authors are solely responsible for the study design; collection, analysis and interpretation of data; writing the report; and a decision to submit the paper for publication.

RESULTS

Overall mortality in the cohort

The mean age of the 1,523 individuals in the study cohort was 55 years (range 30-91 years), and 72% were females. Among the 1,523 subjects, 92 (6.0%) died over the subsequent 5 years. Eight of 25 health conditions were found associated with 5year mortality rates of 19% or more, and were classified as "acutely life-threatening diseases," i.e., coronary artery disease, other heart diseases, chronic kidney disease, chronic bronchitis, chronic leg ulcers, diabetes, cancer and stroke. The 17 other conditions with subsequent 5-year mortality rates of 17% or less were classified as "non-acutely life-threatening diseases," i.e., hypertension, peptic ulcer, inflammatory gut disease, asthma, thyroid disease, Parkinson's disease, epilepsy, other neurologic diseases, chronic back pain, fibromyalgia, psoriasis, psychiatric diseases, alcoholism, osteoarthritis, musculoskeletal trauma, rheumatoid arthritis and ankylosing spondylitis.

The 92 deaths included 8 of 429 (1.9%) who had reported no health condition, 21 of 728 (2.9%) with a non-acutely life-threatening condition, and 63 of 366 (17.2%) with one or more acutely life-threatening conditions (Table 1) (some patients had 2 or 3 such conditions, so total mortality was less than 19%). The 8 subjects with no health condition and 21 with no acutely life-threatening conditions were pooled for further mortality analyses as 29 (2.5%) of 1,157 subjects with no condition or no acutely lifethreatening condition who died within 5 years. The mean baseline age of all patients who survived or died over the 5-year period was 54 and 75 years, respectively (p. <0.001) (Table 2), including 51 and 69 years in subjects with no conditions or no acutely life-threatening conditions (p <0.001), and 65 and 77 years in subjects with an acutely life-threatening condition (p <0.001).

Survival according to four medical history variables

Cumulative survival in the entire cohort differed according to physical function scores: 98% with scores <1 (on a 0-3 scale) survived versus 93% with scores ≥1 (Figure 2). Survival was 99% in those with pain VAS scores ≤4 versus 97% in those with pain scores >4. Survival was >99% in those who exercised more than once weekly, 97% in those who exercised once weekly, and 93% in those who did not exercise. Survival was 98% in non-smokers versus 95% in smokers (Figure 2). Further analyses of survival according to each of the four variables are presented below.

Physical function scores and mortality risk

Mean physical function scores were 0.27 (on a scale of 0–3) in all subjects, including 0.20 in those who survived and 1.4 in those who died over the 5-year period (p <0.001) (Table 2). In the 1,257 subjects with no conditions or no acutely life-threatening conditions, mean physical function scores were 0.16, including 0.13 for those who survived and 1.1 for those who died (p <0.001) (Table 2). In the 366 subjects with acutely life-threatening conditions, mean physical function scores were 0.63, including 0.45 in those who survived and 1.5 in those who died (p <0.001) (Table 2). The hazard ratio and 95% confidence interval (CI) for mortality over 5 years for physical function scores ≥1 (on a scale of 0–3), was 3.5 (95% CI: 2.1–5.1) for all subjects, 4.5 (95% CI:

1.6–12.6) for those with non-acutely life-threatening conditions, and 3.1 (95% CI: 1.8–5.5) for those with acutely life-threatening conditions (Table 3).

Pain scores and mortality risk

The mean pain score was 20 (on a scale of 0–100) in all subjects, including a mean level of 19 in those who survived compared to 38 in those who died over the next 5 years (p <0.001) (Table 2). The mean pain score in individuals with no condition or no acutely life-threatening condition was 16, including 16 in those who survived compared to 27 in those who died (p = 0.020) (Table 2). The mean pain score in subjects with an acutely life-threatening condition was 34, including 32 in those who survived compared to 43 in those who died over the next 5 years (p = 0.008). The hazard ratio (with 95% CI) for mortality over 5 years if pain scores were >40 compared to \leq 40 (on a scale of 0–100) was 2.2 (95% CI: 1.3–3.5) for all subjects (Table 3), 3.1 (95% CI: 1.2–8.3) for those with non-acutely life-threatening conditions, but 1.5 (95% CI: 0.9–2.8) for those with acutely life-threatening conditions, not meeting the p<0.05 criterion (p <0.16).

Exercise frequency and mortality risk

Among all individuals, 28% exercised less than once per week, including 26% of those who survived and 76% of those who died over the 5 years (Table 2). Among subjects with no conditions or no acutely life-threatening conditions, 25% exercised less than once per week, including 24% who survived versus 63% who died (Table 2).

Among subjects who had an acutely life-threatening condition, 40% exercised less than once per week, including 33% who survived and 82% who died. The hazard ratio (with

95% CI) for death over 5 years among subjects who exercised less than once per week compared to those who did exercise at least once per week was 5.2 (95% CI: 3.1–8.9) for all subjects, 4.9 (95% CI: 1.8–13) for those with non-acutely life-threatening conditions, and 4.7 (95% CI: 2.3–9.6) for those who had an acutely life-threatening condition (p <0.001 for all comparisons) (Table 3).

Smoking and mortality risk

Current smoking was reported by 17% of subjects, including 17% who survived versus 19% who died over the 5-year period (p=0.61) (Table 2). Among those with no condition or no acutely life-threatening condition, 19% were smokers, including 18% who survived versus 28% who died (p=0.27). Among those who had acutely life-threatening conditions, 13% were smokers, including 12% who survived versus 15% who died (p = 0.59). Among all subjects, people who smoked at baseline had a 4.6-fold higher hazard ratio (95% CI: 2.5–8.6) to die within 5 years compared to nonsmokers (p <0.001), including a hazard ratio of 7.4 (95% CI: 2.1–25) among people with a condition that was not acutely life-threatening, and 3.3 (95% CI: 1.5–7.3) among those who had an acutely life-threatening condition (Table 3).

Multivariate Cox regression analyses

The four variables studied are not independent, and multivariate regression analyses were performed (Table 4). In the entire cohort, physical function, exercise and current smoking were each significant independent predictors of 5-year mortality, while pain was not significant, i.e., explained by the other variables (Table 4). In individuals

younger than age 55 who had no acutely life-threatening condition, pain and smoking were significant independent predictors of mortality, and physical function and exercise were not significant; no medical history variable was significant in multivariate analyses. In individuals 55 years old and older who had no acutely life-threatening condition, functional status was the only significant predictor of mortality, whereas both functional status and lack of exercise (but not pain or smoking) were independent statistically significant predictors in individuals over age 55 who had an acutely life-threatening condition (Table 4).

DISCUSSION

The results confirm and extend a number of reports (only some of which are cited here) that poor physical function ¹⁻⁷, pain ^{3, 8-10}, limited exercise ^{11, 12}, and smoking ¹⁴ predict premature mortality. Smoking ¹⁴ and limited exercise ^{11, 12, 29} are more widely recognized as predictors of premature death than poor physical function ^{2, 7} and pain ^{3, 9, 10}. Nonetheless, these four medical history variables usually are not collected in everyday medical care – even smoking status often remains unknown ³⁰, although some evidence of improvement has been reported ³¹. By contrast, variables from sources other than the medical history with similar prognostic significance for premature mortality – such as blood pressure and cholesterol – are collected rigorously in most clinical care and health maintenance settings.

The new information presented here is that prognostic quantitative data concerning physical function, pain, exercise status and smoking can be collected in a format found on a 1-page (2-sided) self-report MDHAQ (Figure 1), which has been

care for 20-30 years ¹⁸⁻²¹, and in many other settings. This questionnaire is given to each patient to complete upon registration for a visit and easily completed by patients in 5-10 minutes, so that collection of the medical history variables involves no additional effort on the part of a health professional or office staff.³² The MDHAQ can be adapted to any clinical, health maintenance, or research setting, and can be completed at home.

In the reported cohort of 1,523 older people from the general Finnish population, survival was 93% in subjects who reported poor physical function or limited exercise, compared to 95% in smokers, 97% in those who reported pain, and 91% in those who reported hypertension, versus 98-99% in other subjects. It could be suggested that one or more of the four patient history variables, which are correlated with one another, might not be necessary in clinical care. However, clinical care of individual patients necessarily addresses multiple variables that might be correlated significantly but may each contribute incrementally to a poor outcome – e.g., blood pressure, cholesterol, glucose ³³. The possible independent contribution of poor physical function, pain, and limited exercise, as reported in the simple self-report MDHAQ format, to higher mortality rates remains to be characterized further.

Physical function, pain, exercise status and smoking may be regarded as "vital signs" from a medical history for chronic diseases and health maintenance, analogous to traditional vital signs in acute care, such as pulse and temperature. Pain ^{34, 35} and smoking status ¹⁴ have been advocated as "vital signs" ¹³, introducing a concept that a vital sign may be derived from a medical history, rather than from physical examination.

Vital signs often confirm impressions of the clinician, but also provide standard quantitative data, which may be regarded as a type of checklist 36, 37 to be monitored from one encounter to another more accurately than through narrative descriptions. Vital signs that identify risk of premature mortality may provide data to analyze whether interventions to improve variables such as physical function or pain will improve survival, as seen for exercise, smoking, blood pressure, and cholesterol. It may also be desirable to include these medical history variables in research and clinical analyses of any risk factor for long-term mortality, to ascertain the extent to which they may modify biomedical, genetic and physiologic risk factors in prediction of long-term mortality.

Several limitations are seen to this study. No laboratory tests were available – it might be of considerable interest to compare these medical history variables with laboratory tests, such as serum cholesterol, in the prognosis of mortality, and whether a component of the risk may be explained by one or more of the reported medical history variables. All subjects were from Finland, although most data suggest that mortality experience in Finland is similar to that found in most Western countries, and reports from many countries have indicated that each of these variables is prognostic of premature mortality. Furthermore, a 76% response rate to a mailed questionnaire is unlikely in locations outside Finland. Diagnoses were available only from self-report, which can be inaccurate for certain diagnoses ³⁸. Nonetheless, most of the excess risk according to these medical history variables was not seen in patients with acutely lifethreatening diseases, which ironically may be over-reported in many situations.

In conclusion, poor physical dysfunction, pain, limited exercise, and smoking may be identified in a general population as risk factors for premature mortality in a standard

systematic format on a simple patient self-report MDHAQ that has been completed at every visit of every patient to the authors for 20-30 years. This questionnaire can be completed before any visit in usual care, health maintenance, or clinical research, so the information is available for clinical care. More information concerning possible modification of these risk factors through therapeutic intervention could advance the quality of life and longevity in many individuals, and general public health in populations.

Authors' statement of contributions:

Design: Sokka and Pincus

Supervision of Data Collection: Sokka

Analyses: Sokka and Pincus

Preparation of manuscript: Pincus and Sokka

Funding: No specific funding source was available for these studies. The authors are solely responsible for the study design; collection, analysis and interpretation of data; writing the report; and a decision to submit the paper for publication.

Competing interest: Dr. Sokka and Dr. Pincus report no competing interest.

Ethics approval: The study was approved by the Ethics Committees of Jyväskylä Central Hospital and Population Register Centre of Finland.

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Table 1. Prevalence of conditions in older general population. Baseline scores for pain and functional capacity on health assessment questionnaire (HAQ), according to status at 5 years.

Condition	N	%	Mean	% who died				
Condition	.,	70	Age	over 5 years				
Reported acutely life-threatening condition								
Chronic leg ulcer	3	0.2%	78	33%				
Stroke	16	1.0%	71	31%				
Chronic kidney disease	10	0.7%	64	30%				
Chronic bronchitis	17	1.1%	71	29%				
Other heart disease	146	9.6%	69	23%				
Diabetes	103	6.8%	65	23%				
Cancer	74	4.9%	67	22%				
Coronary artery disease	135	8.9%	73	19%				
Reported non-acutely life-	hreatenin	g condition						
Rheumatoid arthritis	58	3.8%	68	17%				
Other neurologic disease	31	2.0%	65	16%				
Parkinson's disease	7	0.5%	70	14%				
Alcoholism	18	1.2%	52	11%				
Epilepsy	10	0.7%	57	10%				
Osteoarthritis	370	24%	66	10%				
Peptic ulcer	67	4.4%	62	10%				
Psychiatric disease	61	4.0%	54	9.8%				
Musculoskeletal trauma	182	11.9%	58	9.3%				
Thyroid disease	99	6.5%	64	9.1%				
Hypertension	454	30%	62	8.8%				
Chronic back pain	373	25%	59	7.2%				
Ankylosing spondylitis	14	0.9%	59	7.1%				
Psoriasis	26	1.7%	55	3.8%				
Asthma	130	8.5%	59	3.1%				
Fibromyalgia	56	3.7%	57	1.8%				
Inflammatory gut disease	19	1.2%	60	0				
No reported conditions	429	28%	47	1.9%				

Table 2. Mean (standard deviation) values for age, physical function and pain, and percentage of patients who exercise rarely or smoke, according to type of condition and vital status 5 years after baseline.

		With no acutely life-		
	All subjects	threatening condition or no condition	With acutely life- threatening condition	
Age in years	7 iii Galajeete	<u> </u>	un outoning condition	
Total	55 (15)	52 (13)	67 (14)	
Alive	54 (14)	51 (13)	65 (13)	
Dead	75 (13)	69 (15)	77 (12)	
p value	<0.001	<0.001	<0.001	
Physical function	n (0-3)			
Total	0.27 (0.60)	0.16 (0.50)	0.63 (0.86)	
Alive	0.20 (0.46)	0.13 (0.35)	0.45 (0.68)	
Dead	1.4 (1.1)	1.1 (1.2)	1.5 (1.1)	
p value	<0.001	<0.001	<0.001	
Pain (0-100)				
Total	20 (24)	16 (21)	34 (29)	
Alive	19 (24)	16 (21)	32 (28)	
Dead	38 (30)	27 (27)	43 (29)	
p value	<0.001	0.015	<0.008	
Exercise <once td="" <=""><td>oer week</td><td></td><td></td></once>	oer week			
Total	28.4%	24.8%	40.3%	
Alive	25.8%	24.0%	32.5%	
Dead	75.9%	62.5%	81.8%	
p value	<0.001	<0.001	<0.001	
Current smoker at baseline				
Total	17.1%	18.5%	12.8%	
Alive	17.0%	18.3%	12.4%	
Dead	19.2%	28.0%	15.1%	
p value	0.61	0.21	0.59	

Table 3. Hazard ratios (95% CI) for 5-year mortality in older general population – analyses adjusted for age and sex.

	% of subjects with poor status	HR (95% CI)	p value*
Physical function ≥1.0 (vs <1.0)	10%	3.5 (2.1 to 5.7)	<0.001
Pain >40 (vs ≤40)	20%	2.2 (1.3 to 3.5)	0.002
Exercise <1 time/week (vs ≥1 time/week)	28%	5.2 (3.1 to 8.9)	<0.001
Current smoking (vs not smoking)	17%	4.6 (2.5 to 8.6)	<0.001

Subjects with no acutely life-threatening conditions

	% of subjects with poor status	HR (95% CI)	p value*
Physical function ≥1.0 (vs <1.0)	5%	4.5 (1.6 to 13)	0.004
Pain >40 (vs ≤40)	14%	3.1 (1.2 to 8.3)	0.024
Exercise <1 time/week (vs ≥1 time/week)	25%	4.9 (1.8 to 13)	0.001
Current smoking (vs not smoking)	18%	7.4 (2.1 to 25)	0.002

Subjects with acutely life-threatening condition

	% of subjects with poor status	HR (95% CI)	p value*
Physical function ≥1.0 (vs <1.0)	25%	3.1 (1.8 to 5.5)	<0.001
Pain >40 (vs ≤40)	40%	1.5 (0.9 to 2.8)	0.16
Exercise <1 time/week (vs ≥1 time/week)	40%	4.7 (2.3 to 9.6)	<0.001
Current smoking (vs not smoking)	13%	3.3 (1.5 to 7.3)	0.003

^{*} adjusted for age and sex

Table 4. Multivariate model: Hazard ratios (95% CI) for 5-year mortality

FIGURE LEGENDS

Figure 1. Multidimensional health assessment questionnaire (MDHAQ). The front page **(A)** includes 10 activities for function, two visual analog scales (VAS) for pain and patient global estimate of status, and a self-report joint count from a rheumatoid arthritis disease activity index (RADAI). Scoring templates for these measures are available on the right-hand side of the page. An index of the three patient-reported measures, routine assessment of patient index data (RAPID3), can be calculated from an MDHAQ in fewer than 10 seconds. The reverse side **(B)** includes a review of systems, fatigue visual analog scale (VAS), recent medical history, queries about change in global status and frequency of exercise, and demographic data (not included in scoring, but providing useful data in clinical care).

Figure 2. Kaplan Meier survival for mortality according to **A)** functional capacity (HAQ ≥1 vs. <1), **B)** pain (>4.0 vs. ≤4.0), **C)** frequency of physical exercise and **D)** smoking status, over 5 years.

Multi-Dimensional Health Assessment Questionnaire (R808-NP2)

This questionnaire includes information not available from blood tests, X-rays, or any source other than you. Please try to answer each question, even if you do not think it is related to you at this time. Try to complete as much as you can yourself, but if you need help, please ask. There are no right or wrong answers. Please answer exactly as you think or feel. Thank you.

					FOR OFFICE
OVER THE LAST WEEK, were you able to:	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do	1.a-j FN (0-10):
a. Dress yourself, including tying shoelaces and doing buttons?	0	1	2	3	
b. Get in and out of bed?	0	1	2		1=0.3 16=5.3 2=0.7 17=5.7
c. Lift a full cup or glass to your mouth?		1			3=1.0 18=6.0
d. Walk outdoors on flat ground?	0	1	2		4=1.3 19=6.3 5=1.7 20=6.7
e. Wash and dry your entire body?	0	1	2		6=2.0 21=7.0 7=2.3 22=7.3
f. Bend down to pick up clothing from the floor?	0	1	2		8=2.7 23=7.7 9=3.0 24=8.0
g. Turn regular faucets on and off? h. Get in and out of a car, bus, train, or airplane?	0	1	2		10=3.3 25=8.3 11=3.7 26=8.7
i. Walk two miles or three kilometers, if you wish?	0	<u>i</u>	2		12=4.0 27=9.0 13=4.3 28=9.3
j. Participate in recreational activities and sports	0	1	2	-	15-4.5 28-9.5 14-4.7 29-9.7 15-5.0 30-10
as you would like, if you wish?					2 PM (0.40):
k. Get a good night's sleep?l. Deal with feelings of anxiety or being nervous?	0	1.1		.23.3 .2 3.3	
m. Deal with feelings of depression or feeling blue?	0	1.1		.2 3.3	
mine can man recimings on depression on reciming state.					
2. How much pain have you had because of you Please indicate below how severe your pai			E PAST W	EEK?	4.PTGL (0-10):
NO O O O O O O O O O O					
PAIN 0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5	6.0 6.5 7.0 7.1	5 8.0 8.5 9.0	9.5 10 IT	COULD BE	RAPID 3 (0-30)
					1011 15 0 (0 00)
3. Please place a check $()$ in the appropriate	spot to indi	icate the a	mount of i	oain vou	
are having today in each of the joint areas				,	
None Mild Moderate Severe		Non	e Mild I	Moderate Severe	Cat:
a. LEFT FINGERS 0 0 1 0 2 0 3	i. RIGHT FI	NGERS	0 🗆 1	2 3	HS = >12
<u>b. LEFT WRIST</u> □ 0 □ 1 □ 2 □ 3	j. RIGHT W	RIST	0 🗆 1	□ 2 □ 3	
c. LEFT ELBOW 0 0 1 0 2 0 3	k. RIGHT EI	BOW	0 🗆 1	□ 2 □ 3	
d. LEFT SHOULDER 0 0 1 0 2 3	I. RIGHT SH	IOULDER	0 🗆 1	2	LS = 3.1-6
e. LEFT HIP	m. RIGHT H	<u>IIP</u> □	0 🗆 1	□ 2 □ 3	R = <3
<u>f. LEFT KNEE</u>	n. RIGHT K		0 🗆 1		
g. LEFT ANKLE 0 0 1 0 2 0 3	o. RIGHT A		-		
<u>h. LEFT TOES</u> □ 0 □ 1 □ 2 □ 3	p. RIGHT T	OES		□2 □3	
<u>q. NECK</u> □ 0 □ 1 □ 2 □ 3	r. BACK		0 🗆 1	□ 2 □ 3	
4. Considering all the ways in which illness a	nd health c	anditions n	ay affect	you at this	
time, please indicate below how you are doing:					
VERY 0 0 0 0 0 0 0 0 0 0 0	0000	000	0 0 VE	RY	
WELL 0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5	6.0 6.5 7.0 7.1	5 8.0 8.5 9.0	9.5 10 PC	ORLY	

Please turn to the other side

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Figure 1. Multidimensional health assessment questionnaire (MDHAQ). The front page (A) includes 10 activities for function, two visual analog scales (VAS) for pain and patient global estimate of status, and a self-report joint count from a rheumatoid arthritis disease activity index (RADAI). Scoring templates for these measures are available on the right-hand side of the page. An index of the three patient-reported measures, routine assessment of patient index data (RAPID3), can be calculated from an MDHAQ in fewer than 10 seconds. The reverse side (B) includes a review of systems, fatigue visual analog scale (VAS), recent medical history, queries about change in global status and frequency of exercise, and demographic data (not included in scoring, but providing useful data in clinical care).

215x279mm (300 x 300 DPI)

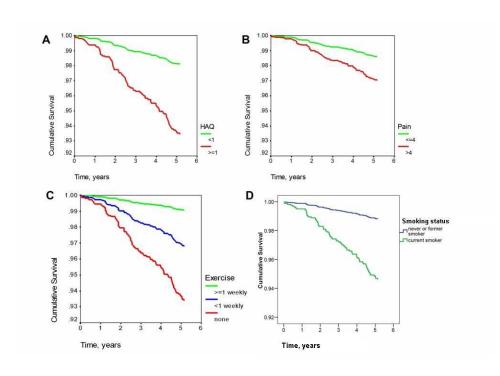


Figure 2. Kaplan Meier survival for mortality according to A) functional capacity (HAQ \geq 1 vs. <1), B) pain (>4.0 vs. \leq 4.0), C) frequency of physical exercise and D) smoking status, over 5 years. 88x60mm (300 x 300 DPI)

 Please check (√) if you ha 	ve experienced any of the follow	ing <u>over the last month:</u>	
Fever	Lump in your throat	Paralysis of arms or legs	FOR OFFICE
Weight gain (>10 lbs)	Cough	Numbness or tingling of arms or	
Weight loss (>10 lbs)	Shortness of breath	Fainting spells	USE CIVET
Feeling sickly	Wheezing	Swelling of hands	5. ROS:
Headaches	Pain in the chest	Swelling of ankles	
Unusual fatigue	Heart pounding (palpitations)	Swelling in other joints	
Swollen glands	Trouble swallowing	Joint pain	
Loss of appetite Skin rash or hives	Heartburn or stomach gas Stomach pain or cramps	Back pain Neck pain	
Unusual bruising or bleeding	Nausea	Use of drugs not sold in stores	
Other skin problems	Vomiting	Smoking cigarettes	
Loss of hair	Constipation	More than 2 alcoholic drinks per	day
Dry eyes	Diarrhea	Depression - feeling blue	,
Other eye problems	Dark or bloody stools	Anxiety - feeling nervous	
Problems with hearing	Problems with urination	Problems with thinking	
Ringing in the ears Stuffy nose	Gynecological (female) problems Dizziness	Problems with memory Problems with sleeping	
Stury riose Sores in the mouth	Losing your balance	Sexual problems	
Dry mouth	Muscle pain, aches, or cramps	Burning in sex organs	
Problems with smell or taste	Muscle weakness	Problems with social activities	
Please check	() here if you have had none of	the above over the last month:	
	e morning OVER THE LAST WEEK If "Yes," please indicate the num		
until you are as limber as you		, 5: 1154	
	ompared to ONE WEEK AGO? Ple 2), the Same \square (3), Worse \square (4)		ek ago
. ,,	,, ,,	,	•
one-half hour (30 minutes): ☐ 3 or more times a week (3)	e aerobically (sweating, increased h ? Please check (✓) only one. ☐ 1-2 times per month (1) ☐ Do not exercise regularly (0) ☐ C		
= 12 times per week (2)	= bo not exercise regularly (o) = e	diffice exercise due to disability, flat	idicap (5)
9. How much of a problem ha	s UNUSUAL fatigue or tiredness	been for you OVER THE PAST W	EEK?
	0 0 0 0 0 0 0 0 0 0		IGUE IS A JOR PROBLEM
	ve you had: [Please check $()$]		
□No □Yes An operation or new		☐Yes Change(s) of arthritis or oth	er medication
□No □Yes Medical emergency on □Yes A fall, broken bone, on □Yes A fall, b		☐Yes Change(s) of address ☐Yes Change(s) of marital status	
□No □Yes A rail, broken borie, o □No □Yes An important new sy		☐Yes Change (s) of marital status	quit work rotired
□No □Yes Side effect(s) of any		☐Yes Change of medical insurance	
□No □Yes Smoke cigarettes reg		☐Yes Change of primary care or o	
	ver below, or indicate any other l		ther doctor
Please explain any res ansi	ver below, or indicate any other i	nearth matter that affects you:	
			_
,	IC GROUP: □ Asian, □ Black, □ I		
our Occupation		e number of years of school you h	
Work Status : □ Full-time, □ Pa			10
☐ Homemaker, ☐ Self-Employed	. □Retired, 11	12 13 14 15 16 17 18 19	20
☐ Seeking work, ☐ Other	Please write yo	our weight: lbs. height: _	inches
our Name	Date of Bir	th Today's Date	-
Page 2 of 2 Thank you for co	mpleting this questionnaire to he	lp keep track of your medical ca	re. R808NP2
FOR OFFICE USE ONLY: I have	re reviewed the questionnaire respons	ses.	
Date:	Signature		

215x279mm (300 x 300 DPI)